Unrealized Savings from the Misuse of REMS and Non-REMS Barriers

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EXECUTIVE SUMMARY

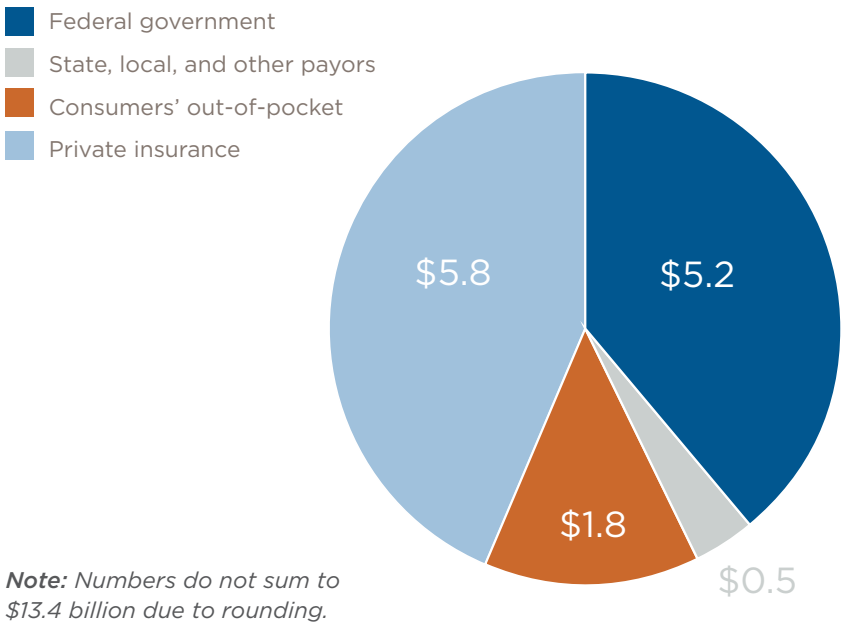
Risk Evaluation and Mitigation Strategies (REMS) are drug safety programs required by the Food and Drug Administration (FDA) for certain high-risk pharmaceuticals. But brand drug manufacturers sometimes use these programs and other forms of restricted access to keep generic manufacturers from obtaining samples needed to develop generic drugs. This practice prevents generic market entry and competition, blocking the cost savings generic drugs are known to deliver.

The Federal Trade Commission has been a vocal critic of REMS misuse and the FDA has recently become more outspoken about REMS misuse and more proactive about preventing it. Misuse of REMS and other restricted access programs has received attention on Capitol Hill as well. In June 2018, the Senate Judiciary Committee passed the bipartisan Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act, legislation that would prevent brand companies from blocking generic firms' access to drug samples.

We estimate that the generic savings lost to the U.S. health care system due to this practice total $13.4 billion annually. The federal government bears more than a third of this burden, or $5.2 billion. Private insurance companies lose $5.8 billion, and consumers pay an extra $1.8 billion in out-of-pocket costs. State and local governments and other small payors lose savings of more than $500 million. Of the total $13.4 billion in lost savings, $3.1 billion is attributable to products restricted by REMS, and $10.3 billion to products with non-REMS restrictions created by brand manufacturers.

As REMS misuse and non-REMS restrictions on drug samples grow, so too do the lost savings. Since our 2014 analysis of this issue, our estimate of lost savings has grown nearly 250 percent. On top of this, misuse of restricted access programs can be expected to affect more biosimilars as their development continues.

$13.4 BILLION IN UNREALIZED SAVINGS, BY PAYOR ($ BILLIONS)



Note: *Numbers do not sum to $13.4 billion due to rounding.*

INTRODUCTION

Risk Evaluation and Mitigation Strategies (REMS) are drug safety programs required by the Food and Drug Administration (FDA) for certain high-risk pharmaceuticals. The intent of REMS programs is to keep patients safe, but brand drug manufacturers use these programs and other forms of restricted access to keep generic manufacturers from obtaining samples needed to develop generic drugs. This practice prevents generic market entry and competition, blocking the cost savings generic drugs are known to deliver. This study, relying on publicly available data from the FDA and a proprietary survey of generic manufacturers, estimates the lost savings to the U.S. health care system from the misuse of REMS and the imposition of similar restrictions on drugs not under REMS.

How REMS Programs Are Used to Block Generic Competition

The Food and Drug Administration Amendments Act of 2007 (FDAAA) granted the FDA the authority to institute REMS programs for small-molecule drugs and biologics. One component of a REMS, known as elements to assure safe use (ETASU), can mandate various types of restrictions on product distribution. Of the 74 existing REMS, 46 include ETASU.[1]

While intended to ensure patient safety, REMS distribution restrictions are sometimes used by brand drug manufacturers to thwart Abbreviated New Drug Application (ANDA) applicants' access to a reference listed drug (RLD). To receive FDA approval for an ANDA, a generic manufacturer must test the generic product it is developing against a sample of the RLD to ensure bioequivalence. If a brand manufacturer can prevent a generic company from accessing a sample, generic competition – and the lower drug prices that come with it – cannot be realized. Preventing ANDA applicants' access to brand drugs for bioequivalence testing and development thus results in lost savings to consumers, private payors, and the federal government.

In addition to using REMS to deny access to samples, brand drug manufacturers have been known to intentionally fail to cooperate with an ANDA applicant regarding the REMS distribution system. The FDA strongly prefers that brand and generic firms establish a shared REMS and will only permit distinct systems if a waiver is granted, a rare occurrence. This, therefore, presents an additional opportunity to restrict generic entry. As the Federal Trade Commission (FTC) describes:

> If the branded and generic firms cannot reach agreement over the terms of a shared REMS, the generic will not be approved unless the FDA grants a waiver for the generic to establish its own REMS distribution system. In practice, the FDA has rarely granted a waiver of the shared REMS requirement, which can create a strategic incentive for the branded firm to refuse to cooperate with the generic entrant, since lack of cooperation can delay generic entry.[2]

Even without a REMS in place, brand manufacturers use restrictions that resemble REMS to block generic access to samples. FDA Commissioner Scott Gottlieb recently highlighted this practice, noting, "We understand that brand companies have placed restrictions in their commercial contracts or agreements with prescription drug distributors, wholesalers or specialty pharmacies that limit the ability of these intermediaries in the drug supply chain to sell samples to generic drug developers for testing."[3]

Policymaker Concerns about REMS Misuse

The FTC has been a vocal critic of REMS misuse. In 2014, the agency cautioned, "If brand firms are able to block generic competition by denying access to the product samples needed to obtain FDA approval, this conduct may prevent the Hatch-Waxman framework from functioning as Congress intended." In July 2017 Congressional testimony, the FTC called REMS misuse "an appropriate area for Congressional focus and concern" and warned that "use of a restricted distribution system to exclude generic competition is especially troubling because it can potentially delay entry indefinitely."[5] Most recently, in the FTC's July 2018 comment on the Department of Health and Human Services Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs, the FTC urged "carefully considered regulatory and legislative efforts to address REMS abuses."[6]

Under Commissioner Gottlieb's direction, the FDA has become more outspoken about REMS misuse and more proactive about preventing it. In November 2017, Gottlieb took a clear stance on the issue, stating, "I consider these tactics unfair and exploitative practices, and they're in direct conflict with our broader public health goals."[7] In May 2018, Gottlieb announced the publication of a list of RLD sponsors and their brand drugs that generic firms reportedly have been unable to access.[8]

Misuse of REMS and other restricted access programs has received attention on Capitol Hill as well. In March 2017, the House Oversight Committee's Subcommittee on Healthcare, Benefits, and Administrative Rules held a hearing on how voluntary restricted distribution systems are used to preempt generic competition. The House Judiciary Committee's antitrust subcommittee held a hearing in July 2017, which featured testimony from Commissioner Gottlieb, on antitrust concerns related to the FDA approval process. In June 2018, the Senate Judiciary Committee passed the bipartisan Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act, legislation that would prevent brand companies from blocking generic firms' access to drug samples.

Biosimilars and Restricted Access

Biologics are among the most expensive pharmaceutical products available today, and they are ripe for the type of restricted access misuse this paper discusses. Made from living cells, biologics cannot be precisely copied the way small-molecule drugs can be. Biosimilars, which have been available for 12 years in Europe, are lower-cost, clinically similar alternatives to biologics. While a regulatory pathway was created in the United States in 2010 for biosimilars to come to market, progress has been slow. Thus far, the FDA has approved 12 biosimilars, and only 4 are on the market. A number of barriers – including those related to reference biologic manufacturers, biosimilar manufacturers themselves, other stakeholders, and the existing legal and policy framework – hinder robust biosimilar competition. Misuse of REMS and restricted access programs constitutes one such barrier. With biologics comprising nearly $120 billion in U.S. drug sales in 2017, misuse of restricted access programs for these products has enormous implications.

Lost Generic Drug Savings from REMS Misuse

In 2014, we estimated that the U.S. health care system could save $5.4 billion annually if REMS were not used to block generic market entry.[9] Here, we update this estimate by analyzing brand products for which generic market entry is currently delayed by abuse of REMS or other restricted access programs. For this analysis, we used a two-prong

approach to identify restricted drugs: a proprietary survey we conducted and the recently published FDA list of RLD sponsors that have reportedly restricted access to samples. We further restricted the data based on criteria discussed below and, using the following methodology, calculated how much could be saved if generic versions of the remaining products were able to come to market. In both the 2014 analysis and the current one, we estimate savings to the overall health care system assuming there are no other barriers to generic entry.

Data

As mentioned above, the products analyzed in this paper were identified by one or both of two sources: 1) the FDA list of brand drugs that generic firms have reported being unable to access,[10] and 2) a survey conducted in June 2018 by Matrix Global Advisors (MGA) of generic drug manufacturers who are members of the Association of Accessible Medicines.

In compiling the list of brand drugs for analysis, MGA removed 1) all duplicates – that is, products that more than one company reported or products that were both on the FDA list and reported on the survey; 2) any drug that had one or more ANDA approved; and 3) products for which sales data were not available in the national health care database run by IQVIA. In the end, our analysis comprised 45 small-molecule drugs and 2 biologics. Sixteen of these products are subject to REMS programs; for the other 31 drugs, non-REMS restrictions are used to block access to samples.

For each of the 47 identified drugs, we obtained U.S. sales for the most recent 12 months (June 2017–May 2018) from all sales channels available through IQVIA. Total U.S. sales for the 47 products analyzed were approximately $18.8 billion in this period. The largest product had 12-month sales of roughly $3.5 billion, and the median product had sales of approximately $91 million. The top four products constituted roughly 50 percent of sales.

We also used publicly available data from the National Health Expenditure Accounts for calendar year 2016 (the latest year for which data are available) to break down our estimate of lost savings by payor.

Methodology

To model the lost savings from brand manufacturers blocking generic access to the 47 identified products, we estimate a generic price discount and the expected generic substitution rate — that is, the share of prescriptions that would be filled with a generic product if one were on the market. We assume a generic substitution rate of 95 percent for small-molecule products, and a biosimilar substitution rate of 30 percent for biologics. For price discounts, we assume an 85 percent discount for drugs with sales over $1 billion, an 80 percent discount for drugs with sales between $200 million and $1 billion, a 70 percent discount for drugs with sales under $200 million, and a 30 percent discount for biologics.

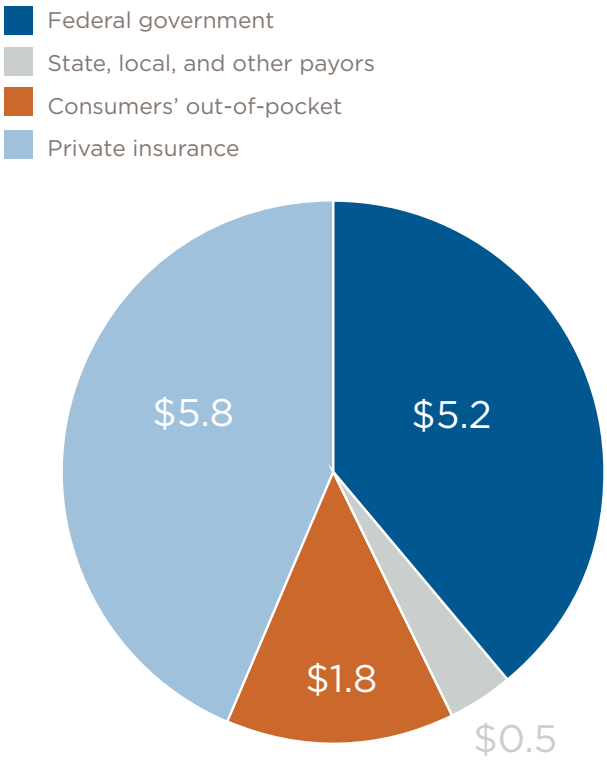
Using the IQVIA sales data from June 2017–May 2018, we calculate lost savings by multiplying sales for each of the identified products by the respective price discount and substitution rate. It should be noted that the estimates of lost savings for these products are conservative because IQVIA data do not include all sales channels. In fact, seven products that would have been included in this analysis (that is, they were reported restricted and had no ANDA approved) were excluded only because of lack of sales data.

Results

We estimate that REMS misuse and restricted access to delay generic market entry for the 47 products in our analysis result in $13.4 billion in lost savings to the U.S. health care system annually. The federal government bears more than a third of this burden, or $5.2 billion. Private insurance companies

lose $5.8 billion, and consumers pay an extra $1.8 billion in out-of-pocket costs. State and local governments and other small payors lose savings of more than $500 million. (**See Chart 1.**)

CHART 1: $13.4 BILLION IN UNREALIZED SAVINGS, BY PAYOR ($ BILLIONS)



Note: *Numbers do not sum to $13.4 billion due to rounding.*

Among government health care programs, Medicare, which accounts for 29 percent of total U.S. prescription drug spending, experiences lost savings of $3.9 billion annually. The economic cost to Medicaid (both federal and state) totals $1.4 billion. Of the total $13.4 billion in lost savings, $3.1 billion is attributable to products restricted by REMS with ETASU, and $10.3 billion to products with non-REMS restrictions created by brand manufacturers.

Since our 2014 analysis, the problem of brand drug companies' misuse of REMS and other restricted access programs has grown nearly 250 percent. While some products that were restricted in 2014 did not appear in our dataset in 2018, new products have been added and the total number of products that we analyzed increased from 40 to 47. Moreover, annual sales from the drugs in our analysis increased substantially. For example, 11 drugs in the current analysis have 12-month sales over $500 million, compared to 5 drugs in our 2014 analysis in this category. Four of the drugs in this analysis with sales over $500 million have seen sales more than triple in the intervening years. On top of this, REMS misuse can be expected to affect more biosimilars as they continue to receive FDA approval.

Conclusion

Government, consumers, and private payors are missing out on sizeable health care savings from the misuse of REMS programs. Specifically, REMS and non-REMS strategies to restrict access to brand drug samples represent lost savings of $13.4 billion annually. As REMS and non-REMS misuse grows, so too do the lost savings. In addition, if misuse extends to more biologics, potential lost savings on biosimilars would be enormous. As this paper illustrates, curbing the misuse of REMS programs would yield demonstrable health care savings.

SOURCES

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ABOUT MGA

MGA is an economic policy consulting firm in Washington, DC. Founded by Alex Brill in 2007, MGA specializes in fiscal, health care, and tax policy matters.

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